REMARKS

Claims 1-18 and 20-28 are pending. Claims 1 and 24 has been amended. Support for the amendments can be found in the application as filed, for example, at page 8, lines 5-8 and page 37, Example 2. No new matter has been added.

Withdrawn Objection

Applicants thank the Examiner for withdrawing the previously-raised objection to the Abstract.

Withdrawn Rejections

Applicants thank the Examiner for withdrawing the 35 U.S.C. §§ 102 and 103 rejections that were raised in an earlier Office Action.

Information Disclosure Statement

Applicants thank the Examiner for considering all of the references listed in the Information Disclosure Statement filed on January 26, 2006.

Objection to Claim Identifiers

The Office at page 2 indicates that the claim identifiers for canceled claims 29-38 should read "Canceled." Claims 29-38 have been labeled accordingly. Withdrawal of this objection is respectfully requested.

35 U.S.C. § 102

The Office at pages 3-7 of the Office Action alleges that claims 1-4, 8, 9, 13, 15-17, and 20-27 are anticipated by U.S. Pat. No. 5,403,484 ("Ladner"). Applicants respectfully disagree and traverse this rejection.

Claim 1. As part of its rejection of claim 1, the Office alleges at page 4:

> [A]s in step (e), the previous infection reaction produced by 348 plaques which were pooled for further affinity selection with the immobilized HNE-beads, and as in step (f), the non-binding phage are separated from the phage bound to the HNE-beads ..."

Applicants submit that the Office has mischaracterized the method of claim 1 and the disclosure of the Ladner reference.

A non-limiting example of the method of claim 1 is provided in Example 2 of the application. As stated in Example 2 on page 37:

> A target protein that includes a nickel chelating tag was contacted to a phage display library that displays Fabs. The mixture was then bound to nickel magnetic beads. After washing the beads three times, XL1 Blue MRF' cells were contacted to the beads. Phage produced by these cells were allowed to bind to the target protein on the beads. The XL1 Blue MRF' cells were removed. The phage-target-bead complexes were washed to remove unbound phage. For a second round of amplification, fresh XL1 Blue MRF' cells were contacted to the beads.

In contrast, the method described in Ladner differs from the method of claim 1. For example, as stated in col. 144, lines 17-36:

> We added $1.1 \cdot 10^8$ plaque forming units of the KLMUT library to 10 µl of a 50% slurry of agarose-immobilized human neutrophil elastase beads (HNE from Calbiochem cross-linked to Reacti-Gel.TM. agarose beads from Pierce Chemical Co. following manufacturers directions) in TBS/BSA. Following 3 hours incubation at room temperature, the beads were washed and phage was eluted as done in the selection of EpiNE phage isolates (Example IV). The progression in lowering pH during the elution was: pH 7.0, 6.0, 5.0, .4.5, 4.0, 3.5, 3.0, 2.5, and 2.0. Beads carrying phage remaining after pH 2.0 elution were used to infect XL1-BlueTM cells that were plated to allow plaque formation. The 348 resulting plaques were pooled to form a phage population for further affinity selection. A population of phage particles containing $6.0 \cdot 10^8$ plaque forming units was added to 10 µl of a 50% slurry of agarose-immobilized HNE beads in TBS/BSA and the above selection procedure was repeated. (emphasis added)

As this excerpt makes clear- and as the Office itself states- in Ladner, plaques from the infected cells were pooled together and subjected to further affinity selection with fresh target alone. In contrast, step (f) recites "separating replicate phage that do not bind to the target of step (a) from the replicate phage immobilized to the support" (emphasis added). Thus, Ladner fails to teach step (f) of claim 1. For at least this reason, Ladner fails to anticipate claim 1 and its dependencies, claims 2-4, 8, 9, 13, and 15-17.

Claim 20. In making its rejection of claim 20, the Office in part alleges at page 5:

> As in independent claim 20, Ladner teaches ...
> [(d)] amplifying members of the subset under at least one of the following conditions (1) fewer than 5000 progeny phage are produced for each phage member selected in step (b)- Ladner teaches the use of the MB phage which is an M13 phage (col. 118, lines 5-33)- Ladner teaches that these phage typically produce between 100 and 1000 progeny (col. 55, lines 40-44) ..."

Applicants respectfully disagree with the Office's conclusions. Lines 40-44 at col. 55 of Ladner merely indicate that M13 phage have a burst size of 100-1000 progeny. However, more

progeny can be produced after the burst, e.g., depending on how long a culture is incubated. For example, the Office also cites col. 118, lines 5-33. As indicated therein:

> A unique NarI site was introduced into codons 17 and 18 of gene III (changing the amino acids from H-S to G-A, Cf. Table 110). 10^6 phage produced from bacterial cells harboring the M13-MB1/2-delta RF DNA were used to infect a culture of CJ236 cells (relevant genotype: F', dut1, ung1, Cm^R) (OD595=0.35) (col. 118, lines 21-26; emphasis added).

As this example from Ladner demonstrates, M13 phage produced 10^6 progeny. Clearly, M13 infection can result in greater than 5000 progeny. Further, the Office relies on the example at col. 144 of Ladner, but that example does not indicate the number of phage progeny produced therein. Thus, for at least these reasons, Ladner does not necessarily describe the method of claim 20, and thus fails to anticipate claim 20 and its dependencies, claims 21-23.

Claim 24. The Office alleges that Ladner anticipates claim 24. Applicants respectfully disagree with the Office's allegations. However, solely in the interest of expediting prosecution, step (iv) of claim 24 has been amended to recite:

> iv) producing phage from the infected cells in the presence of the target, the produced phage being replicates of phage that bind to the target, wherein
> (1) fewer than 5000 progeny phage are produced for each phage that infects one of the host cells,
> (2) the producing is completed in less than 4 hours, or
> (3) the cells divide less than seven times.

Applicants submit that Ladner fails to anticipate amended claim 24 and its dependencies, claims 25-27. Withdrawal of this rejection is respectfully requested.

35 U.S.C. § 103

Ladner and Anderson

The Office at pages 7-9 of the Action alleges that claims 1-9, 13, 15-17, and 20-27 are obvious in light of Ladner and Anderson (U.S. Pat. No. 6,649,419).

In making its rejection, the Office sets forth why it believes the combination of Ladner and Anderson renders claims 5, 6, and 7 *prima facie* obvious (Applicants assume that the Office is also rejecting claim 1 on this basis as claims 5, 6, and 7 depend from claim 1).

Regarding claims 1 and 5-7: As discussed above, Ladner does not teach or suggest producing replicate phage from the infected cells in the presence of the target immobilized support to produce replicate phage immobilized to the target of step (a) or separating replicate phage that do not bind the target of step (a). The Office has not indicated how Anderson

remedies such deficiencies, and Applicants submit that Anderson fails to remedy the deficiencies of Ladner. As a result, claim1 and its dependencies, claims 5-7, are non-obvious in light of Lander and Anderson.

Regarding claims 2-4, 8, 9, 13, 15-17, and 20-27: The Office fails to set forth any rationale as to why it believes the combination of Ladner and Anderson renders claims 2-4, 8, 9, 13, 15-17, and 20-27 *prima facie* obvious. Thus, Applicants respectfully submit that, if a subsequent Office Action that rejects claims 2-4, 8, 9, 13, 15-17, and 20-27 as allegedly being obvious in light of Ladner and Anderson is issued, such an Office Action cannot be made final as Applicants have not had the opportunity to address the merits of a *prima facie* obviousness rejection of these claims in light of these references.

Withdrawal of this rejection is respectfully requested.

Ladner and Janda

At pages 9-10, the Office alleges that claims 1-4, 8-10, 12-17, and 20-28 are obvious in light of Ladner and Janda (U.S. Pat. No. 5,571,681).

In the Action, the Office indicates why it believes this combination of references renders claims 10, 12, and 14 (and presumably claim 1) *prima facie* obvious.

Regarding claims 1, 10, 12, and 14: Ladner does not teach or suggest producing replicate phage from the infected cells in the presence of the target immobilized support to produce replicate phage immobilized to the target of step (a) or separating replicate phage that do not bind the target of step (a). The Office has not indicated how Janda remedies these deficiencies. Further, Applicants submit that Janda fails to remedy the deficiencies of Ladner. As a result, claims 1 10, 12, and 14, are non-obvious in light of Lander and Janda.

Regarding claims 2-4, 8, 9, 13, 15-17, and 20-28: The Office does not set forth any rationale as to why it believes the combination of Ladner and Janda renders claims 2-4, 8, 9, 13, 15-17, and 20-28 *prima facie* obvious. Thus, Applicants respectfully submit that, if a subsequent Office Action that rejects claims 2-4, 8, 9, 13, 15-17, and 20-28 as allegedly being obvious in light of these references is issued, such an Office Action cannot be made final as Applicants have not had the opportunity to address the merits of a *prima facie* obviousness rejection of these claims in light of these references.

Applicants respectfully request that this rejection be withdrawn.

Ladner and McCafferty

The Office at pages 10-11 alleges that claims 1-4, 8, 9, 13, 15-18, and 20-27 are obvious in light of Ladner and McCafferty (U.S. Pat. No. 5,969,108).

In making its rejection, the Office sets forth its rationale regarding why the combination of Ladner and McCafferty allegedly renders claim 18 *prima facie* obvious (implicitly rejecting claim 1 on this basis as claim 18 depends from claim 1).

Regarding claims 1 and 18: Ladner does not teach or suggest producing replicate phage from the infected cells in the presence of the target immobilized support to produce replicate phage immobilized to the target of step (a) or separating replicate phage that do not bind the target of step (a). The Office has not set forth how McCafferty remedies such deficiencies. Indeed, Applicants submit that McCafferty fails to remedy the deficiencies of Ladner. As a result, claims 1 and 18 are non-obvious in light of Lander and McCafferty.

Regarding claims 2-4, 8, 9, 13, 15-17, and 20-27: The Office fails to set forth any rationale as to why it believes the combination of Ladner and McCafferty renders claims 2-4, 8, 9, 13, 15-17, and 20-27 *prima facie* obvious. Thus, Applicants respectfully submit that, if a subsequent Office Action rejecting claims 2-4, 8, 9, 13, 15-17, and 20-27 as allegedly obvious in light of Ladner and McCafferty is issued, such an Office Action cannot be made final as Applicants have not had the opportunity to address the merits of a *prima facie* obviousness rejection of these claims in light of these references.

Withdrawal of this rejection is respectfully requested.

Ladner, Janda, and Steinbuchel

At pages 11-12 of the Action, the Office alleges that claims 1-4, 8-17, and 20-28 are obvious in light of Ladner, Janda, and Steinbuchel (U.S. Pat. No. 6,022,729).

In making its rejection, the Office provides its rationale regarding why the combination of Ladner, Janda, and Steinbuchel allegedly render claim 11 (and presumably claim 1) *prima facie* obvious.

Regarding claims 1 and 11: Ladner does not teach or suggest producing replicate phage from the infected cells in the presence of the target immobilized support to produce replicate phage immobilized to the target of step (a) or separating replicate phage that do not bind the

target of step (a). The Office has not indicated how Janda and Steinbuchel remedy these deficiencies, and Applicants submit that Janda and Steinbuchel fail to remedy the deficiencies of Ladner. As a result, claims 1 and 11 are non-obvious in light of Lander, Janda, and Steinbuchel.

Regarding claims 2-4, 8-10, 12-17, and 20-28: The Office does not set forth why it believes the combination of Ladner, Janda, and Steinbuchel renders claims 2-4, 8-10, 12-17, and 20-28 *prima facie* obvious. Thus, Applicants respectfully submit that, if a subsequent Office Action rejects claims 2-4, 8-10, 12-17, and 20-28 as allegedly obvious in light of Ladner, Janda, and Steinbuchel, such an Office Action cannot be made final as Applicants have not had the opportunity to address the merits of a *prima facie* obviousness rejection of these claims in light of these references.

Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants respectfully submit that all of the pending claims are in condition for allowance, which action is expeditiously requested. Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do Applicants concede that there are not other good reasons for patentability of the presented claims or other claims.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, please charge any deficiency to Deposit Account No. 50/2762.

Respectfully submitted,
Ladner et al., *Applicant*

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